WHAT IS CLAIMED IS:

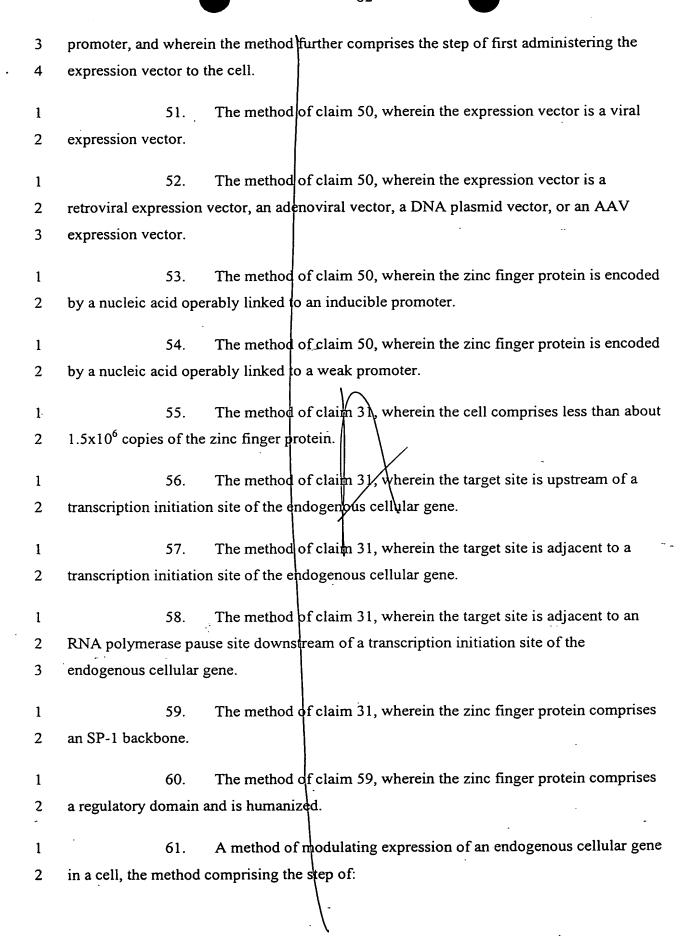
1	1. A method of inhibiting expression of an endogenous cellular gene
2	in a cell, the method comprising the step of:
3	contacting a first targed site in the endogenous cellular gene with a first
4	zinc finger protein, wherein the K _d of the zinc finger protein is less than about 25 nM;
5	thereby inhibiting expression of the endogenous cellular gene by at least
6	about 20%.
1	2. The method of claim 1, wherein the step of contacting further
2	comprises contacting a second target site in the endogenous cellular gene with a second
3	zinc finger protein.
1	3. The method of claim 2, wherein the first and second target sites are
2	adjacent.
1	4. The method of claim 3 wherein the first and second zinc finger
2	proteins are covalently linked.
1	5. The method of claim 1, wherein the first zinc finger protein is a
2	fusion protein comprising a regulatory domain.
1	6. The method of claim 5, wherein the first zinc finger protein is a
2	fusion protein comprising at least two regulatory domains.
1	7. The method of claim 2, wherein the first and second zinc finger
2	proteins are fusion proteins, each comprising a regulatory domain.
1	8. The method of claim 7, wherein the first and second zinc finger
2	protein are fusion proteins, each comprising at least two regulatory domains.
1	9. A method of inhibiting expression of an endogenous cellular gene
2	in a cell, the method comprising the step of:
3	contacting a target site in the endogenous cellular gene with a fusion zinc
4	finger protein comprising six fingers and a regulatory domain, wherein the K _d of the zinc
5	finger protein is less than about 25 nM;

6	thereby inhibiting expression of the endogenous cellular gene by at least		
7	about 20%.		
1	10. The method of claim 1, wherein the cell is selected from the group		
2	consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.		
1	11. The method of claim 10, wherein the cell is a mammalian cell		
1	12. The method of claim 11, wherein the cell is a human cell		
1	13. The method of claim 1, wherein expression of the endogenous		
2	cellular gene is inhibited by at least about 75%-100%.		
1	14. The method of claim 1, wherein the endogenous cellular gene is a		
2	selected from the group consisting of VEGF, ERa, IGF-I, c-myc, c-myb, ICAM, and		
3	Her2/Neu.		
1	15. The method of claim 1, wherein the endogenous cellular gene is		
2	VEGF.		
1	16. The method of claim 1, wherein the inhibition of gene expression		
2	prevents gene activation.		
1	17. The method of claim 5 or 7, wherein the regulatory domain is		
2	selected from the group consisting of a transcriptional repressor, an endonuclease, a		
3	methyl transferase, and a histone deacetylase.		
1	18. The method of claim 1, wherein the method further comprises the		
2	step of first administering to the cell a delivery vehicle comprising the zinc finger protein		
3	wherein the delivery vehicle comprises a liposome or a membrane translocation		
4	polypeptide.		
1	19. The method of claim 1, wherein the zinc finger protein is encoded		
2	by a zinc finger protein nucleic acid operably linked to a promoter, and wherein the		
3	method further comprises the step of first administering the nucleic acid to the cell in a		
4	lipid:nucleic acid complex or as naked nucleic acid.		

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1	20. The method of claim 1, wherein the zinc finger protein is encoded		
2	by an expression vector comprising a zinc finger protein nucleic acid operably linked to a		
3	promoter, and wherein the method further comprises the step of first administering the		
4	expression vector to the cell.		
	21. The method of claim 20, wherein the expression vector is a viral		
1			
2	expression vector.		
1	22. The method of claim 20, wherein the expression vector is a		
2	retroviral expression vector, an adenoviral expression vector, a DNA plasmid expression		
3	vector, or an AAV expression vector.		
,	23. The method of claim 20, wherein the zinc finger protein is encoded		
1	\ \ \ \ \		
2	by a nucleic acid operably linked to an inducible promoter.		
1	24. The method of claim 20, wherein the zinc finger protein is encoded		
2	by a nucleic acid operably linked to a weak promoter.		
	of the definite the cell comprises less than about		
1	25. The method of claim 1, wherein the cell comprises less than about		
2	1.5x10 ⁶ copies of the zinc finger protein		
1	26. The method of claim 1, wherein the target site is upstream of a		
2	transcription initiation site of the endogenous cellular gene.		
1	27. The method of claim 1, wherein the target site is adjacent to a		
2	transcription initiation site of the endogenous cellular gene.		
1	28. The method of claim 1, wherein the target site is adjacent to an		
2	RNA polymerase pause site downstream of a transcription initiation site of the		
3	endogenous cellular gene.		
1	29. The method of claim 1, wherein the zinc finger protein comprises		
2	an SP-1 backbone.		
1	30. The method of claim 29, wherein the zinc finger protein comprises		
2	a regulatory domain and is humanized.		
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1		31.	A method of activa	ting expression of an endogenous cellular gene,
2	the method comprising the step of:			
3		contac	ting a first target sit	in the endogenous cellular gene with a first
4	zinc finger pro	otein, w	herein the K _d of the	zinc finger protein is less than about 25 nM;
5		thereby	y activating express	ion of the endogenous cellular gene to at least
6	about 150%.			
1		32.	•	m 31, wherein the step of contacting further
2	comprises contacting a second target site in the endogenous cellular gene with a second			
3	zinc finger pro	otein.		
1		33.	The method of claim	m 32, wherein the first and second target sites
2	are adjacent.	55.		,
۷	are adjacent.			
1	•	34.	The method of cla	m 33, wherein the first and second zinc finger
2	proteins are co	ovalentl	y linked.	
1		35 .		im 31, wherein the first zinc finger protein is a
2	fusion protein	compri	sing a regulatory do	omain.
1		36.	The method of cla	im 35, wherein the first zinc finger protein is a
2	fusion protein	compri	sing at least two reg	gulatory domains.
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1		37.	The method of cla	im 32, wherein the first and second zinc finger
2	proteins are fi	ısion pr	oteins, each compri	sing a regulatory domain.
1		38.	The method of cla	im 37, wherein the first and the second zinc
2	finger protein			omprising at least two regulatory domains.
۷	imger protein	are rus	ion proteins, each o	Simplify at least two regulatory decisions
1		39.	A method of activ	ating expression of an endogenous cellular gene,
2	the method co	mprisir	ng the step of:	
3		contac	ting a target site in	he endogenous cellular gene with a fusion zinc
4	finger protein	compri	sing sin fingers and	a regulatory domain, wherein the K _d of the zinc
5	finger protein	is less	than about 25 nM;	
6		thereb	y activating express	ion of the endogenous cellular gene to at least
7	about 150%.			

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1	40.	The method of claim 3	l, wherein the cell is selected from the
2	group consisting of	of an animal cell, a plant cell	l, a bacterial cell, a protozoal cell, or a
3	fungal cell.		
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1	41.	The method of claim 40), wherein the cell is a mammalian cell.
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1	42.	Ine method of claim 4	l, wherein the cell is a human cell
1	43.	The method of claim 3	l, wherein expression of the endogenous
2	cellular gene is ac	tivated to at least about 200	-500%.
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1	44.	The method of claim 3	l, wherein the endogenous cellular gene is a
2	selected from the	group consisting of FAD2 1	, EPO, GM-CSF, GDNF, VEGF, and LDL-
3	R.		h
1	45.	The method of claim 3	l, wherein the endogenous cellular gene is
2	VEGF.		
1	46.	The method of claim 3	1, wherein the activation of gene expression
1			, wherein the activation of gene expression
2	prevents repressio	on of gene expression.	
1	47.	The method of claim 3	5 or 37, wherein the regulatory domain is
2	selected from the	group consisting of a transc	riptional activator, or a histone
3	acetyltransferase.		•
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1	48.	The method of claim 3	, wherein the method further comprises the
2	step of first admir	nistering to the cell a deliver	vehicle comprising the zinc finger protein,
3	wherein the delive	ery vehicle comprises a lipo	some or a membrane translocation
4	polypeptide.		
1	40	The method of claim 2	, wherein the zinc finger protein is encoded
1	49.		
2			linked to a promoter, and wherein the
3	<i>:</i>		ninistering the nucleic acid to the cell in a
4	lipid:nucleic acid	complex or as naked nucleio	c àcid.
1	50.	. The method of claim 3) 1, wherein the zinc finger protein is encoded
2	by an expression	vector comprising a zinc fin	ger protein nucleic acid operably linked to a
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3	contacting a first target site in the endogenous cellular gene with a first
4	zinc finger protein;
5	thereby modulating expression of the endogenous cellular gene.
1	62. The method of claim 61, wherein the step of contacting further
2	comprises contacting a second target site in the endogenous cellular gene with a second
3	zinc finger protein.
1	63. The method of claim 62, wherein the first and second target sites
2	are adjacent.
1	64. The method of claim 63, wherein the first and second zinc finger
2	proteins are covalently linked.
1	65. The method of claim 61, wherein the first zinc finger protein is a
2	fusion protein comprising a regulatory domain.
1	66. The method of claim 65, wherein the first zinc finger protein is a
2	fusion protein comprising at least two regulatory domains.
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1	67. The method of claim 62 wherein the first and second zinc finger
2	proteins are fusion proteins, each comprising a regulatory domain.
1	68. The method of claim 67, wherein the first and second zinc finger
2	protein are fusion proteins, each comprising at least two regulatory domains.
1	69. A method of modulating expression of an endogenous cellular gen
2	in a cell, the method comprising the step of:
3	contacting a target site in the endogenous cellular gene with a fusion zinc
4	finger protein comprising six fingers and a regulatory domain;
5	thereby modulating expression of the endogenous cellular gene.
1	70. The method of claim 61, wherein the cell is selected from the
2	group consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal
3	cell.
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1	71. The method of claim 70 , wherein the cell is a mammalian cell





1	72. The method of claim /1, wherein the cell is a numan cell.
1	73. The method of claim 61, wherein the endogenous cellular gene is a
2	selected from the group consisting of VEGF, ERa, IGF-I, c-myc, c-myb, ICAM,
3	Her2/Neu, FAD2-1, EPO, GM-CSF, GDNF, and LDL-R.
1	74. The method of claim 61, wherein the endogenous cellular gene is
2	VEGF.
1	75. The method of claim 65 or 67, wherein the regulatory domain is
2	selected from the group consisting of a transcriptional repressor, a transcriptional
3	activator, an endonuclease, a methyl transferase, a histone acetyltransferase, and a histone
4	deacetylase.
1	76. The method of claim 61, wherein the method further comprises the
2	step of first administering to the cell a delivery vehicle comprising the zinc finger protein,
3	wherein the delivery vehicle comprises a liposome or a membrane translocation
4	polypeptide.
1	77. The method of claim 61, wherein the zinc finger protein is encoded
2	by a zinc finger protein nucleic acid operably linked to a promoter, and wherein the
3	method further comprises the step of first administering the nucleic acid to the cell in a
4	lipid:nucleic acid complex or as naked nucleic acid.
1	78. The method of claim 61, wherein the zinc finger protein is encoded
2	by an expression vector comprising a zinc finger protein nucleic acid operably linked to a
3	promoter, and wherein the method further comprises the step of first administering the
4	expression vector to the cell.
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1	79. The method of claim 78, wherein the expression vector is a viral
2	expression vector.
1	80. The method of claim 78, wherein the expression vector is a
2	retroviral expression vector, an adenoviral expression vector, a DNA plasmid expression
3	vector, or an AAV expression vector.

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1	-81.	The method of claim 78, wherein the zinc finger protein is encoded
2	by a nucleic acid ope	rably linked to an inducible promoter.
1	82.	The method of claim 78, wherein the zinc finger protein is encoded
2	by a nucleic acid ope	erably linked to a weak promoter.
1	83.	The method of claim 61, wherein the cell comprises less than about
2	1.5x10 ⁶ copies of the	zinc finger protein.
1	84.	The method of claim 61, wherein the target site is upstream of a
2	transcription initiation	on site of the endogenous cellular gene.
1	85.	The method of claim 61, wherein the target site is adjacent to a
2	transcription initiation	on site of the endogenous cellular gene.
1	86.	The method of claim 61, wherein the target site is adjacent to an
2	RNA polymerase par	use site downstream of a transcription initiation site of the
3	endogenous cellular	gene.
1	87.	The method of claim 61, wherein the zinc finger protein comprises
2	an SP-1 backbone.	
1	88.	The method of claim 88, wherein the zinc finger protein comprises
2	a regulatory domain	and is humanized.
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